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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/925,664	08/09/2001	Dan W. Denney JR.	GENTIOPE-06499	3389

23535 7590 06/17/2003

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/925,664	DENNEY, DAN W.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I in Paper No. 13 is acknowledged. Claims 1-20 and 27-32 are canceled without prejudice or disclaimer.

2. Therefore, claims 21-32 are pending and examined on the record.

Claim Rejections - 35 USC § 112, 1st paragraph

3. Claims 21-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating B-cell lymphoma comprising the administration of a multivalent anti-idiotypic antibody or multivalent compound comprising at least two heavy chain variable regions or two light chain variable regions, it does not reasonably provide enablement for a method of treating B-cell lymphoma comprising the administration of a multivalent vaccine comprising at least two heavy chain variable regions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn to a method of treating B-cell lymphomas in a patient with a multivalent vaccine, derived from the tumor cells of the patient, which comprises at least two heavy chain variable regions. The claims are also further limited to a method further comprising the administration of adjuvants or conjugation of the vaccine to carrier proteins.

The instant invention at the time of filing was based on an improved method of treating B-cell lymphomas, wherein the improvement involved overcoming somatic

mutations associated with B-cell lymphomas. To overcome this problem, the applicant's have disclosed a method to produce a library of variable regions found on B-cells lymphomas in a fast and effective manner so as to optimize the chances of inducing an immune response against the lymphomas. Such a method involves PCR amplification using primers to conserved sequences that flank the CDR regions on the gene of the Ig molecule found on the surface of B-cell lymphomas. Following amplification, cloning into an expression vector comprising constant regions, and purification of the multivalent product (anti-idiotypic antibody), the anti-idiotypic is administered to the patient suffering from B-cell lymphomas.

The art teaches that the treatment of B-cell lymphomas is often challenging and difficult depending on the stage of disease. One such examples McCormick *et al* (PNAS USA 1999 Jan;96:703-708) teach that most B-cell lymphomas are incurable, and that the tumors are variable in terms of treatment and prognosis. Furthermore, the art also teaches that the use of vaccines in the treatment of cancer is not feasible and also difficult. One such example, Evans *et al* (Q. J. Med 1999;92:29-307) teaches that there is a lack of definitive data showing the effectiveness of vaccines to prevent cancer as it relates to preventing disease and in advanced disease. No wherein in the art does it teach how vaccines are to be administered for cancer as a prophylactic regimen to prevent the formation of cancer.

The working examples of the instant invention have only taught how to administer the multivalent compound or antibody as a treatment of B-cell lymphoma. There is no indication that this is capable of working as a preventative regime, because

there is a lack of data showing how this would be able to prevent the reoccurrence of B-cell lymphoma following initial administration. Furthermore, the method involves the isolation of TAAs from the patient so that the compound used to treat can be manufactured. It is not clear how one would be able to prevent cancer through vaccination with an element derived from a cancer. Further still, the specification has not provided any teachings to the effect of how and why a patient that is immunized with a vaccine for B-cell lymphoma would react with a heightened immune system. Would the patient develop tolerance to the vaccine, would the patient develop any autoimmune diseases, would the patient be able to elicit the correct response in the event B-cell do become malignant? These questions are critical in understanding whether the claimed method is feasible as a method of treating B-cell lymphomas. In addition, there is no way one of skill in the art would be able to predetermine which subjects within a population would require the administration of a vaccine, because to date, there are no tests that can be used to determine whom amongst the population would develop B-cell lymphoma. Therefore, given the lack of teaching with regard to the use of a vaccine and absent any teachings to overcome the unpredictability in the art, one of skill in the art would be forced to determine numerous factors in order to practice the instant invention.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevenson FK *et al* (Meeting abstract, Gene Therapy of Cancer: 2nd European Conference, September 7-8, 1995, London, A14). Claims are drawn to a method of treating a B-cell lymphoma comprising the administration to a subject having a B-cell lymphoma, a multivalent vaccine comprising at least two recombinantly produced heavy chains differing by at least one idiotype. Stevenson FK *et al* teach the production of a vaccine that is made up of variable regions derived from tumor biopsies and administering those variable regions to a murine lymphoma mouse model. Those variable regions consisted of scFv which are made up of both heavy and light chains.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stevenson *et al* in view of Kwak *et al* (N. Engl. J. Med. 1992 Oct;327(17):1209-15). Claims are drawn to a method of treating B-cell lymphoma comprising the administration of a multivalent vaccine comprising at least two recombinant heavy chains, wherein the vaccine further comprises adjuvants or carrier proteins. Stevenson

et al (see paragraph 5, *supra*, for disclosure) however do not specifically teach the use of adjuvants or carrier proteins in combination with the multivalent vaccine.

Kwak *et al* however, teach the use of adjuvants and carrier proteins in combination with a method of treating B-cell lymphoma in a patient using Ig molecules derived from said patient. Kwak *et al* further suggest that the use of adjuvants in this immune response was "essential".

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of filing to treat B-cell lymphomas with a multivalent vaccine comprising at least two recombinant heavy chains or light chains further comprising adjuvants and or carrier proteins. One of ordinary skill would have been motivated to combine the two references because it was already known that B-cell lymphomas could be treated with vaccines comprising a mixture of idiotypic determinants in scFv of which comprises both heavy and light chains and that the combination of that scFv in the treatment of B-cell lymphomas could be combined with adjuvants and carrier proteins because Kwak *et al* teach that it was an important factor in the treatment. One of skill in the art would have expected a reasonable amount of success in combining the methods or teachings because Kwak *et al* disclosed a method of treating B-cell lymphomas with adjuvants and carrier proteins and states that such combinantion was critical for the success of the treatment.

Conclusion

8. No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
June 16, 2003

ANTHONY C. CAPUTA
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